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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/529,028	03/24/2005	Sarina Striem	800.1019	9002

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EXAMINER	
OH, TAYLOR V	

ART UNIT	PAPER NUMBER
1625	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/529,028	STRIEM ET AL.	
	Examiner	Art Unit	
	Taylor Victor Oh	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 January 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) *1-8,10 and 16-31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9,11,13 and 15* is/are rejected.

7)☒ Claim(s) *12 and 14* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *24 March 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/24/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

The Status of Claims:

Claims 1-31 are pending.

Claims 9 and 11,13,15 are rejected.

Claims 1-8, 10, and 16-31 are withdrawn from consideration.

Claims 12 and 14 are objected.

DETAILED ACTION

1. Claims 9 and 11-15 are under consideration in this Office Action.

Priority

2. It is noted that this application is a 371 of PCT/IL03/00225 (03/16/2003), which has foreign priority documents, Israel 151921 (09/25/02) .

Drawings

3. The drawings filed on 3/24/05 are accepted by the examiner.

Election/Restriction

Applicant's election with traverse of Group II (claims 9 and 11-15) on 1/30/08 is acknowledged.

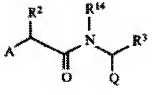
Claims 1-8, 10, and 16-31 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected groups I and III-V there being no allowable generic or linking claims.

Applicants argue in the following:

a. It appears that the '933 patent does not establish that the claims of the present application are directed to separate inventions; in fact, the '933 patent is not related to the claimed subject matter; the compounds in the patent appears to be related to the inhibition of HIV, not to the inhibition of MMPS.

The examiner has noted applicants' argument. However, this is not found persuasive because another patent Xue et al (5,703,093) discloses the followings:

> The present invention provides novel hydroxamic acids and carbocyclic acids and derivatives thereof and to pharmaceutical compositions and methods of use of these novel compounds for the inhibition of matrixmetalloproteinases, such as stromelysin and other matrix metalloproteinases, and also inhibit the production of tumor necrosis factor (TNF), and are therefore useful for the treatment of arthritis and other related inflammatory diseases. These novel compounds are represented by Formula I below:



Formula I

In the instant case, the invention of Group I is directed to the method of inhibiting protease activity using the formula (I), whereas the invention of Group II is directed to the method for preventing, or treating a MMP-related diseases using the formula (I). Both may have commonly shared a compound having the formula I. However, according to Xue et al (5,703,093) , it shows that hydroxamic compounds with an inhibiting protease activity have chemically different structures from the commonly

shared compounds of formula (I) between them. From this, there is no the special technical feature between Groups I and II. Thus, there is no single general inventive concept and no unity of invention for the method or the process as defined in 37 CFR 1.475.

In the instant case, the invention of Group I is directed to the method of inhibiting protease activity using the formula (I), whereas the invention of Group III is directed to the method for preventing, or treating a cancer using the formula (I). Both may have commonly shared a compound having the formula I. However, according to Xue et al (5,703,093) , it shows that hydroxamic compounds with an inhibiting protease activity have chemically different structures from the commonly shared compounds of formula (I) between them. From this, there is no the special technical feature between Groups I and III. Thus, there is no single general inventive concept and no unity of invention for the method or the process as defined in 37 CFR 1.475.

In the instant case, the invention of Group I is directed to the method of inhibiting protease activity using the formula (I), whereas the invention of Group IV is directed to the method for treating angiogenesis using the formula (I).
Both may have commonly shared a compound having the formula I. However, according to Xue et al (5,703,093) , it shows that hydroxamic compounds with an inhibiting protease activity have chemically different structures from the commonly shared compounds of formula (I) between them. From this, there is no the special technical feature between Groups I and IV. Thus, there is no single general inventive

concept and no unity of invention for the method or the process as defined in 37 CFR 1.475.

In the instant case, the invention of Group I is directed to the method of inhibiting protease activity using the formula (I), whereas the invention of Group V is directed to method for preparation of a medicament using the formula (I) and its pharmaceutical composition and compounds. Both may have commonly shared a compound having the formula I. However, according to Xue et al (5,703,093) , it shows that hydroxamic compounds with an inhibiting protease activity has chemically different structures from the commonly shared compounds of formula (I) between them. From this, there is no the special technical feature between Groups I and V. Thus, there is no single general inventive concept and no unity of invention for the method or the process as defined in 37 CFR 1.475. Therefore, the Examiner has a right to restrict them in this case.

The requirement is still deemed proper and is therefore made FINAL.

Claim Objections

Claims 12 and14 are objected to under 37 CFR 1.75(c) as being in improper form because claim 12 and 14 depend on a multiple dependent claim 9. See MPEP § 608.01(n). Accordingly, the claims 12 and 14 are not been further treated on the merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 9 and 11-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 9, the term "general " is recited. This expression is vague and indefinite because the specification does not elaborate what is meant by the term "general ." Appropriate correction is required.

Claim 9 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating specific diseases, does not reasonably provide enablement for preventing diseases. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. Applicants are not enabled for preventing any of these diseases. The only established prophylactics are vaccines not the formula(I) of compounds such as present here. In addition, it is presumed that "prevention" of the claimed diseases would require a method of

identifying those individuals who will develop the claimed diseases before they exhibit symptoms. There is no evidence of record that would guide the skilled clinician to identify those who have the potential of becoming afflicted.

"The factors to be considered [in making an enablement rejection] have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art, and the breadth of the claims", *In re Rainer*, 146 USPQ 218 (1965); *In re Colianni*, 195 USPQ 150, *Ex parte Formal*, 230 USPQ 546. 1) As discussed above, preventing diseases requires identifying those patients who will acquire the disease before any disease occurs. This would require extensive and potentially opened ended clinical research on healthy subjects. 2) The passage spanning line 15,page 8 to line 2, page 9 lists the diseases Applicant intend to treat. 3) There is no working example of such a preventive procedure in man or animal in the specification. 4) The claims rejected are drawn to MMP-related diseases and are therefore physiological in nature. 5) The state of the art is that no general procedure is art-recognized for determining which patients generally will become preventive before the fact. 6) The artisan using Applicants invention would be a Board Certified physician in MMP-related diseases with an MD degree and several years of experience. Despite intensive efforts, pharmaceutical science has been unable to find a way of getting a compound to be effective for the prevention of MMP-related diseases generally. Under such circumstances, it is proper for the PTO to require evidence that such an

unprecedented feat has actually been accomplished, *In re Ferens*, 163 USPQ 609. No such evidence has been presented in this case. The failure of skilled scientists to achieve a goal is substantial evidence that achieving such a goal is beyond the skill of practitioners in that art, *Genentech vs. Novo Nordisk*, 42 USPQ2nd 1001, 1006. This establishes that it is not reasonable to any agent to be able to prevent MMP-related diseases generally. That is, the skill is so low that no compound effective generally against MMP-related diseases has ever been found let alone one that can prevent such conditions. 7) It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved", and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). 8) The claims broadly read on all patients, not just those undergoing therapy for the claimed diseases and on the multitude of compounds embraced by Formula (I).

The Examiner suggests deletion of the word "preventing" and the phrase "reducing the risk".

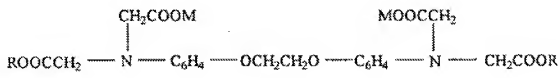
Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 9, 11,13, and 15 are rejected under 35 U.S.C. 102(b) as being anticipated clearly by Kozak et al (WO99/16741).

Kozak et al discloses the followings(see page 9 ,lines 15-26):



Formula 1

wherein the substituents on the aromatic rings are in the ortho position, R is selected from the group consisting of C_nH_{2n+1} (n=1-10), $C_nH_{2n+1}(OCH_2CH_2)_m$ (n=1-20, m=1-6), $(C_nH_{2n+1})_2N(CH_2)_m$ (n=1-6, m=1-6) and substituted or unsubstituted $ArCH_2$; and M denotes any physiologically acceptable cation.

The compounds of the invention may be useful in open heart surgery and for the treatment of medical conditions associated with increased levels of divalent metal ions, in particular calcium. These conditions may include, but are not limited to, brain and cardiac ischemia, stroke, myocardial infarction, epilepsy, chronic neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease and acute inflammation as well as diseases associated with neuronal and muscular hyperactivity such as urinary incontinence, prostatic hypertrophy, muscular spasm, arterial hypertension, asthma and irritable bowel syndrome.

(see page 12 ,lines 3-10). This is identical with the claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Taylor Victor Oh whose telephone number is 571-272-0689. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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3/01/08